EFFECTS OF CHRONIC RENAL FAILURE AND DIALYSIS ON CARDIOVASCULAR SYSTEM

ESSAY

Submitted For Partial Fulfillment
Of Master Degree
In
CARDIOLOGY

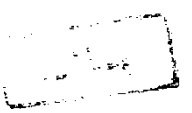
By

MAGDY FAROUK WADII
(M.B., B.Ch.)

Supervisors

PROF. Dr. ALI RAMZY
PROFESSOR OF CARDIOLOGY
AIN SHAMS UNIVERSITY

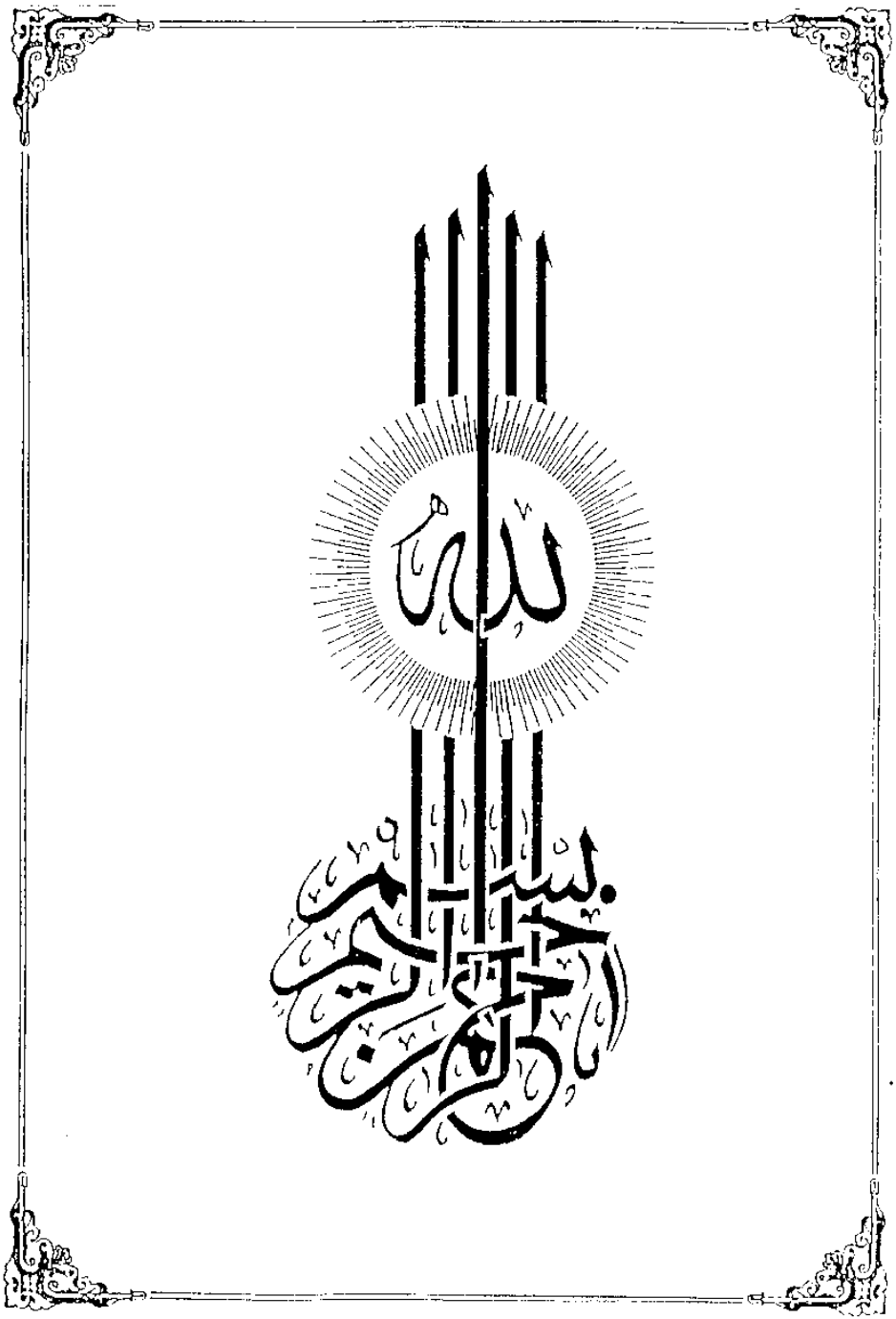
PROF. Dr. AHMED HELAL
PROFESSOR OF CARDIOLOGY
MILITARY MEDICAL ACADEMY



FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

1986

TO MY PARENTS...



ACKNOWLEDGEMENT

With my great pleasure, I wish to acknowledge my indebtedness to Professor Dr. Aly Ramzy, Professor of Cardiology, Ain Shams University, who suggested the idea of this assay, and who kindly and so carefully assisted and collaborated with me. I wish to express my gratitude to him for his close supervision, giving me much of his valuable time and directing me by useful instructions. I have been fortunate to be under his supervision.

I wish to express my sincere gratitude to Professor Dr. Ahmed H. Helal, Professor of Cardiology, Military Medical Academy. Really he is our Godfather. He has been a kind source of virtual sympathetic and wise guidance, that helped me in my carear. My acknowledgement represents an inadequate expression of appreciation to him.

My heartful admiration to Dr. Sayed Abdel Hafiez, M.D. Cardiology, for his useful advice and actual help. To him I am so greatful because he put all the facilities near my hand.

To Dr. Ismail Sabry, Assistant Professor of Cardiology, Military Medical Academy, I wish to express my gratitude for his kind help. He gave me a lot of time to collect, write and finish this work beside lot of advice. My heartful thanks to him.

REVIEW OF LITERATURE

CHAPTER 1.

ALTERATION IN CARDIOVASCULAR PHYSIOLOGY IN RENAL FAILURE

conduction and produces profound alterations in the surface electrocardiogram. Severe hyperkalemia may also produce cardiac standstill secondary to markedly impaired intraventricular conduction or, more rarely, ventricular fibrillation (Fisch, I982).

Intrinsic myocardial depressant factors may be present in uremia. The evidence in favour of such factors has been reviewed by Prosser and Parsons (I975), and includes the observation of depressed cardiac contractility in an isolated rat heart preparation perfused with compounds that are elevated in uremia, e.g. urea, creatine, guanidinosuccinic acid and methylguanidine, separately or in combination (Scheuer and Stezoski, I973).

Hypertrophy may alter myocardial function. Cardiac hypertrophy occurs when the heart is subjected to a chronic pressure load, e.g. arterial hypertension, or in conjunction with dilatation when the heart is subjected to a chronic volume load as occurs in anemia, A-V fistula, or aortic regurgitation. Studies on ventricular muscle removed from animals with hypertrophy due to a chronic pressure load showed a decrease in intrinsic contractility (Braunwald, I980).

However, it appears that the intrinsic contractile ability of hypertrophied myocardium from chronically volume-loaded hearts remains near normal unless the load is very large and clinical signs of congestive failure are present (Braunwald, I980).

B. Factors primarily affecting cardiac loading:

1. Hypertension:

Renal disease is frequently accompanied by arterial hypertension. The hypertension of renal failure is often related to volume overload but may also be due to increased renin activity or other factors (Onesti et al., I975). Hypertension affects the heart by increasing the after-load for left ventricular ejection (Cohn et al., I974).

The left ventricle must generate a pressure that exceeds the elevated diastolic pressure before ejection can begin and must develop enough additional pressure during the remainder of systole to eject the stroke volume into the aorta. This elevated systolic pressure increases the left ventricular systolic wall stress and thus the after-load of the left ventricle. As shown in figure 1, this increased after-load shifts

the ventricular output curve downward so that a lower stroke results for a given atrial pressure. If venous return can be augmented by an increase in blood volume or by venoconstriction, the cardiac output can be restored toward normal (Guyton et al., 1973).

Concentric left ventricular hypertrophy is a compensatory structural change induced by hypertension. By the Laplace relationship, an increased left ventricular wall thickness due to hypertrophy helps reduce the increased systolic wall stress produced by elevated arterial pressure. This reduction in systolic wall stress increases the stroke volume produced at any level of pre-load. However, left ventricular hypertrophy produced by chronic pressure overload may also increase diastolic stiffness of the left ventricle, so that for any left atrial pressure, the ventricle distends to a smaller end-diastolic volume. This decreases the end-diastolic fiber stretch, or pre-load, so that the stroke volume falls. Thus hypertrophy exerts two opposing effects on the left ventricular output curve, or the relationship between left atrial pressure and stroke volume. The decrease in systolic wall stress tends to shift the relationship upward toward its normal position, whereas the increased

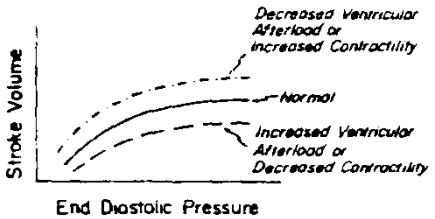


Figure 1: Relationship between stroke volume and end-diastolic pressure when the latter is used as a measure of preload. This relation is frequently referred to as the ventricular output (or function) curve. The curve is shifted upward or downward, depending on the level of afterload and/or intropic state.

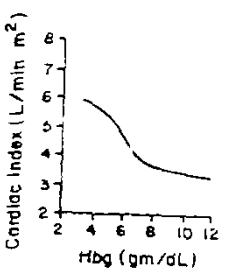


Figure 2: Effect of decreased hemoglobin (Hbg) on cardiac index in patients without renal failure.

A similar relationship between anemia and cardiac output has been observed in patients with renal failure (Neff et al., I97I). An increase in cardiac output occurs as a result of two consequences of anemia: (1) decreased blood viscosity; and (2) decreased blood oxygen-carrying capacity (Fig. 3).

With a decrease in hemoglobin concentration and hematocrit, the blood contains more fluid and fewer formed elements, so that it is less viscous and presents less resistance to flow. This reduced blood viscosity decreases the effective peripheral vascular resistance for any level of arteriolar tone, and thus for any cardiac output, the arterial pressure is lower. This decreases left ventricular systolic wall stress and thus the left ventricular after-load. Decreased left ventricular after-load shifts the ventricular output curve upward, so that any level of pre-load produces a larger stroke volume. Additionally, the decreased blood viscosity decreases the effective resistance to venous return, so that any right atrial pressure is associated with greater venous return (Guyton et al., I973). The upward shifts of both ventricular output and the venous return curves promote an increase in cardiac output. Moreover, the increase in venous

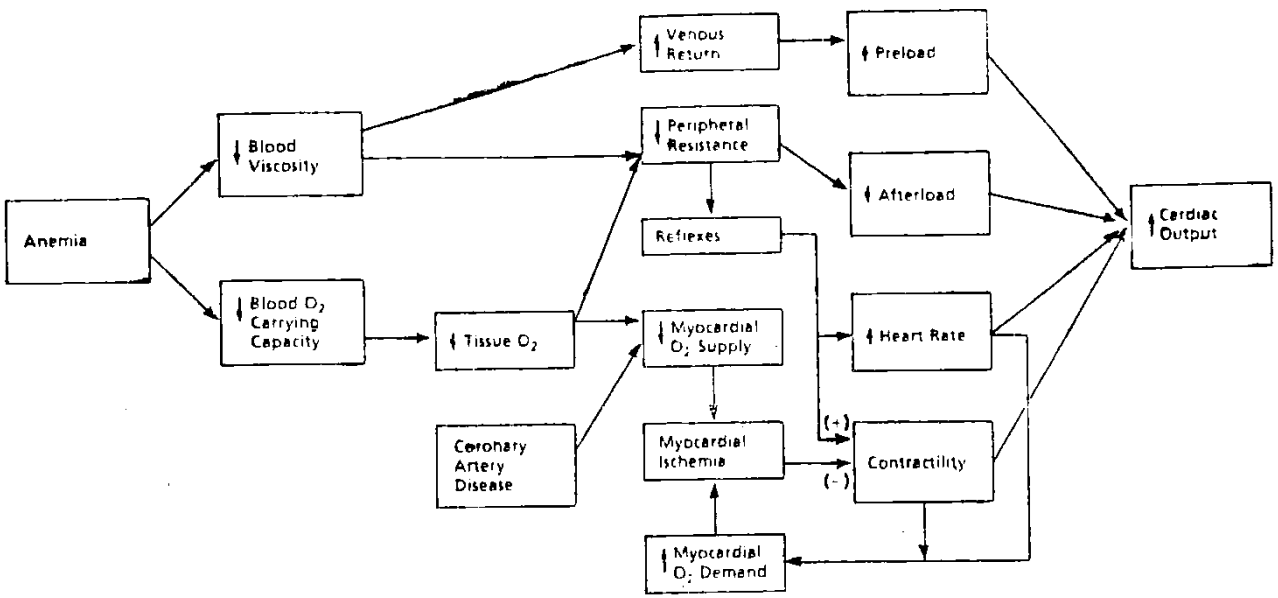


Figure 3 Effect of anemia on the determinants of cardiac output.

return and the fall in blcod pressure (from the decreased peripheral vascular resistance), both trigger autonomic reflexes that increase heart rate and myocardial contractility, further augmenting the output. The importance of these autonomic reflexes was demonstrated by Glick, Plauth and Braunwald (I964), who found that the elevation in cardiac output in response to severe anemia was greater in intact dogs than in animals with chronic cardiac denervation.

The decreased hemoglobin concentration in anemia reduces the oxygen-carrying capacity of the blood. If there is inadequate peripheral compensation by increased tissue oxygen extraction, oxygen delivery to the tissues is reduced and local hypoxia may develop. This results in a decrease in arteriolar tone, increasing the regional blood flow and oxygen delivery. The net effect of vasodilatation in many vascular beds is a decline in total peripheral vascular resistance and a further reduction in left ventricular after-load.

The increased pre-load, the decreased after-load and the reflex-mediated increase in heart rate and contractility all contribute to an increased cardiac output; however, the increased heart rate, contractility

and cardiac output also augment myocardial oxygen demand. At the same time, the decreased oxygen-carrying capacity of the blood may reduce the myocardial oxygen supply beyond the ability of the coronary circulation to match oxygen delivery to oxygen demand. This effect occurs much earlier and is augmented if there is co-existing coronary artery disease.

3. Decreased sodium and fluid excretion:

A decrease in renal sodium and water excretion is a common finding in renal insufficiency and leads to an increase in the intra-vascular blood volume. The increased intra-vascular volume increases the systemic and pulmonary venous volumes and the mean circulatory pressures. The venous return curve is thus shifted upward so that any atrial pressure is associated with a greater venous return. The augmented venous return increases ventricular filling and pre-load, which increases the stroke volume.

Increased right atrial volume may stimulate right atrial stretch receptors, resulting in an increase in heart rate (the Bainbridge reflex). The increased intra-vascular water may dilute the plasma proteins (which may also be depleted in patients with nephrotic

syndrome), decreasing the osmotic pressure. The increased venous pressure in combination with the decreased osmotic pressure, promotes transudation of fluid, which may result in peripheral and pulmonary edema. Pulmonary edema makes the lung stiffer, increasing the work of respiration. The presence of alveolar fluid may interfere with pulmonary oxygen exchange and lead to hypoxia. Severe hypoxia can reduce the myocardial oxygen supply and produces ischemia, which depresses myccardial contractility.

A major effect of sodium and water retention in anephric patients is the production of arterial hypertension (Onesti et al., I975). Restoration of patients to their dry weight frequently returns the arterial pressure to normal. The increase in arterial pressure in response to a sodium and fluid load is primarily due to an elevation of the peripheral vascular resistance (Onesti et al., I975). This increased resistance may be the result of several factors:-

i. Increased sodium may make the arteries more sensitive to angiotensin or other vasoconstrictor substances (Brunner et al., I972).